



## 10 years of livestock-associated MRSA in Denmark: How big is the problem?

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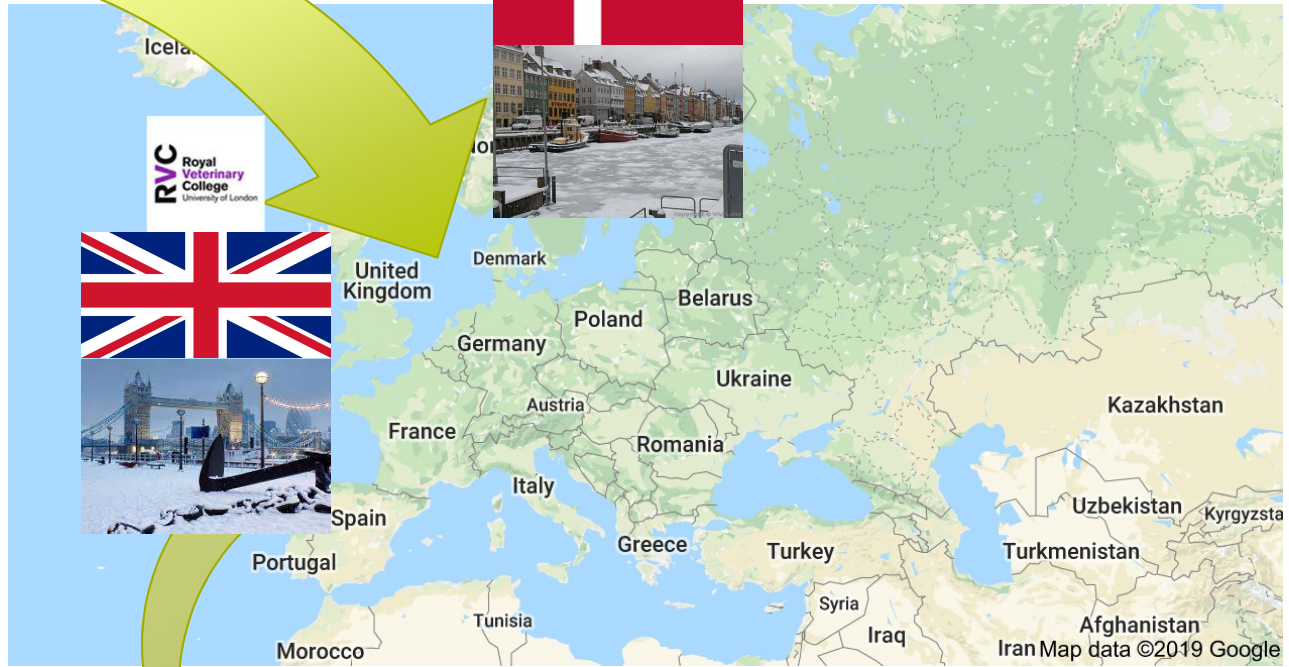
RVC Royal Veterinary College University of London



United Kingdom

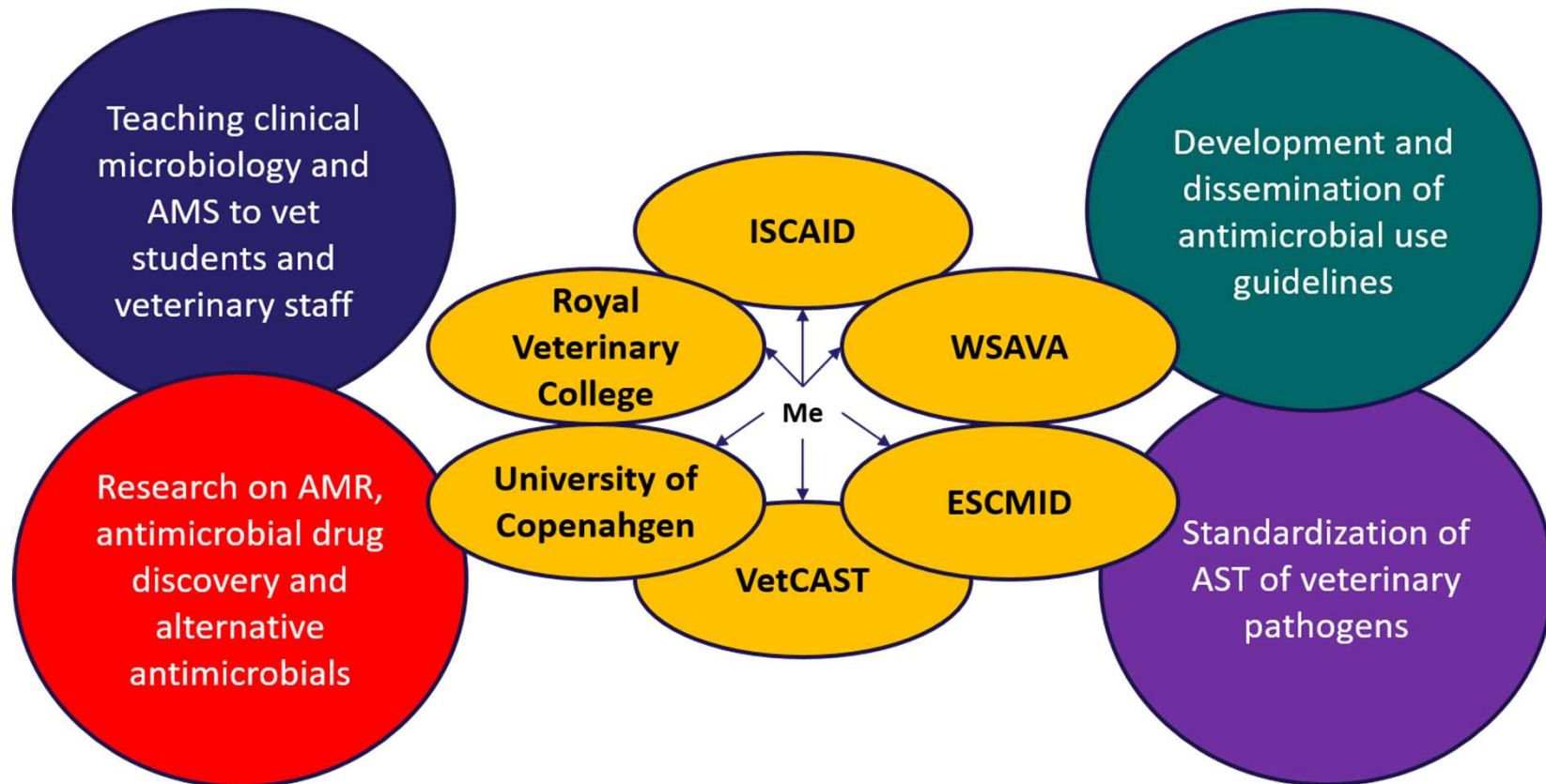


November 2015 - December 2018

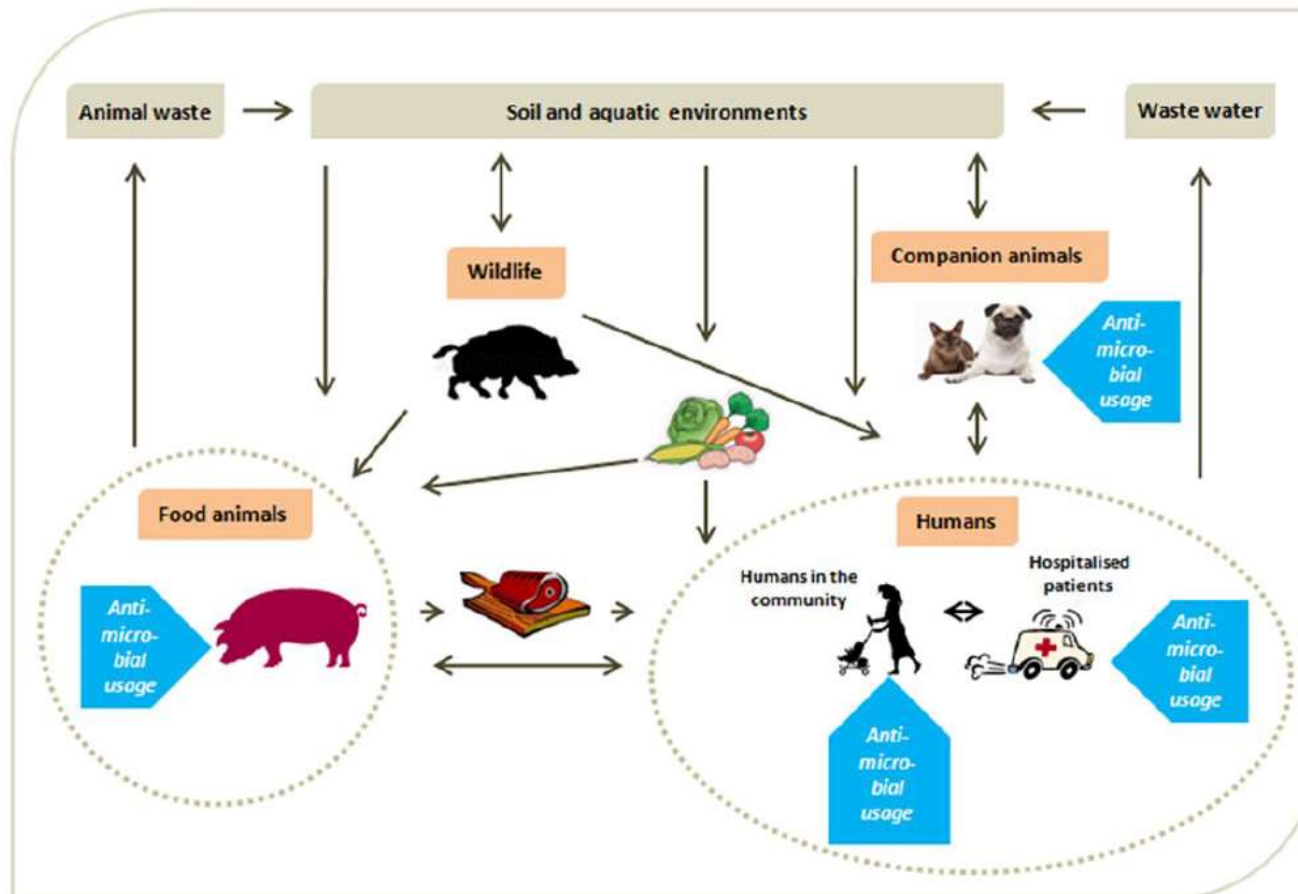


March 2019





## AMR is a One Health problem and its solution requires a One Health approach



## Lecture outline

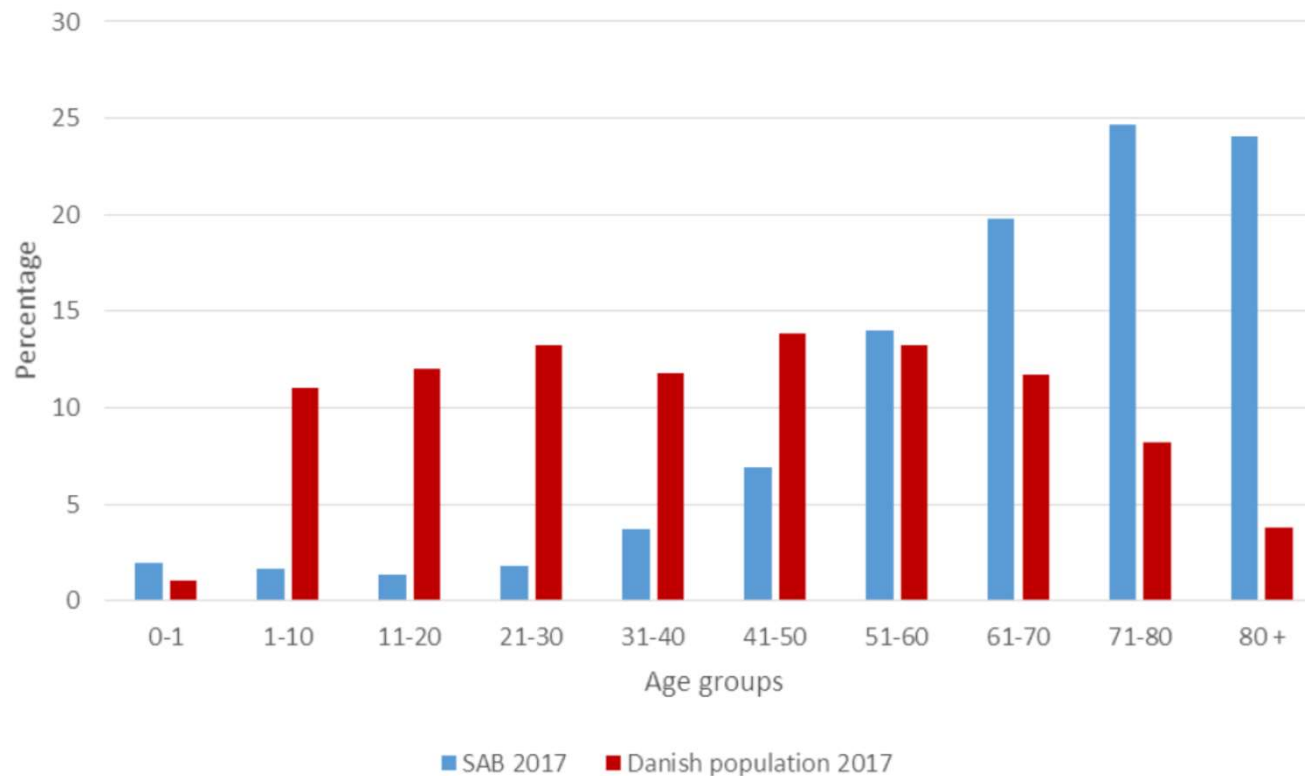
- Intro on *S. aureus* and MRSA
- State-of-the art of LA-MRSA in Denmark
  - MRSA vs LA-MRSA
  - MRSA vs MSSA
  - SA vs other infections
- Answer to the question 😊
- Take-home messages

## What is *S. aureus*?

- A common commensal of the human and animal body (the nasal cavity is the preferential colonization site)
- A minority of the human population is constantly colonized (20-30%)
- Infection is usually ( $\approx 70\%$ ) caused by the colonizing strain
- Infections range from mild (e.g. skin/soft tissue) to severe (e.g. bacteremia)
- Rare pathogen in pigs (mainly subclinical infections) where 3 major clones have been described (**ST398**, ST9 and ST433)



## Age distribution of *S. aureus* bacteraemia patients SAB report 2017



Alderly and patients with other diseases (transplant, haemodialysis and cancer patients) are categories at risk

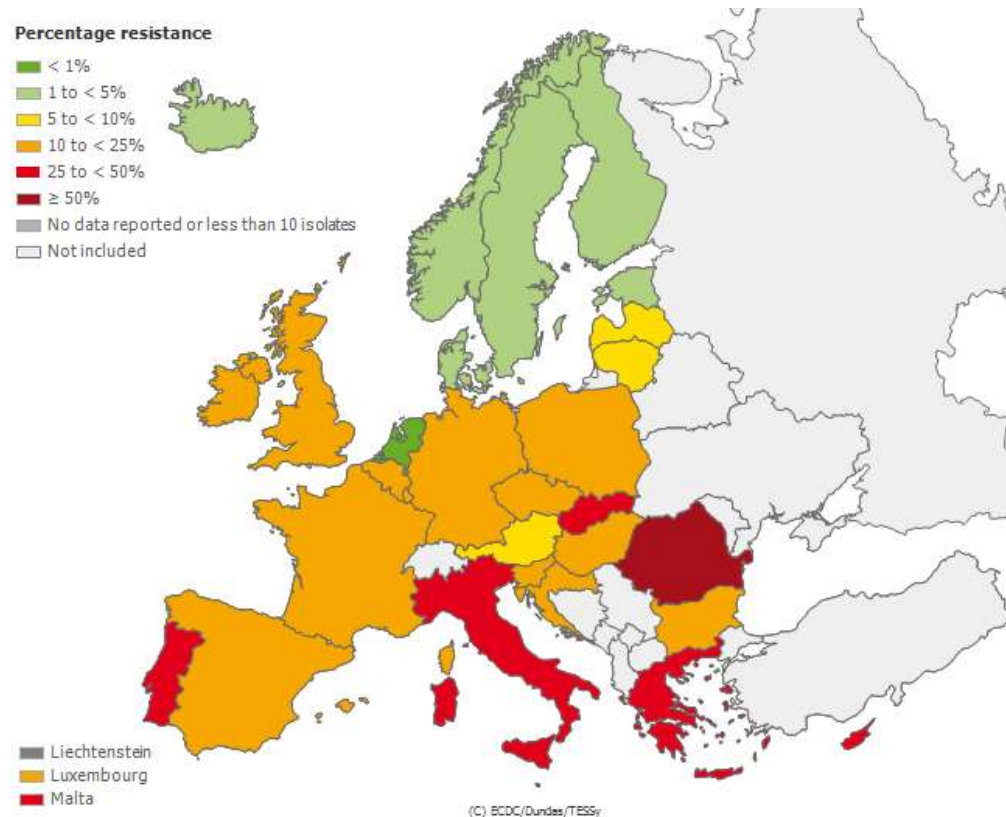
## What is MRSA?



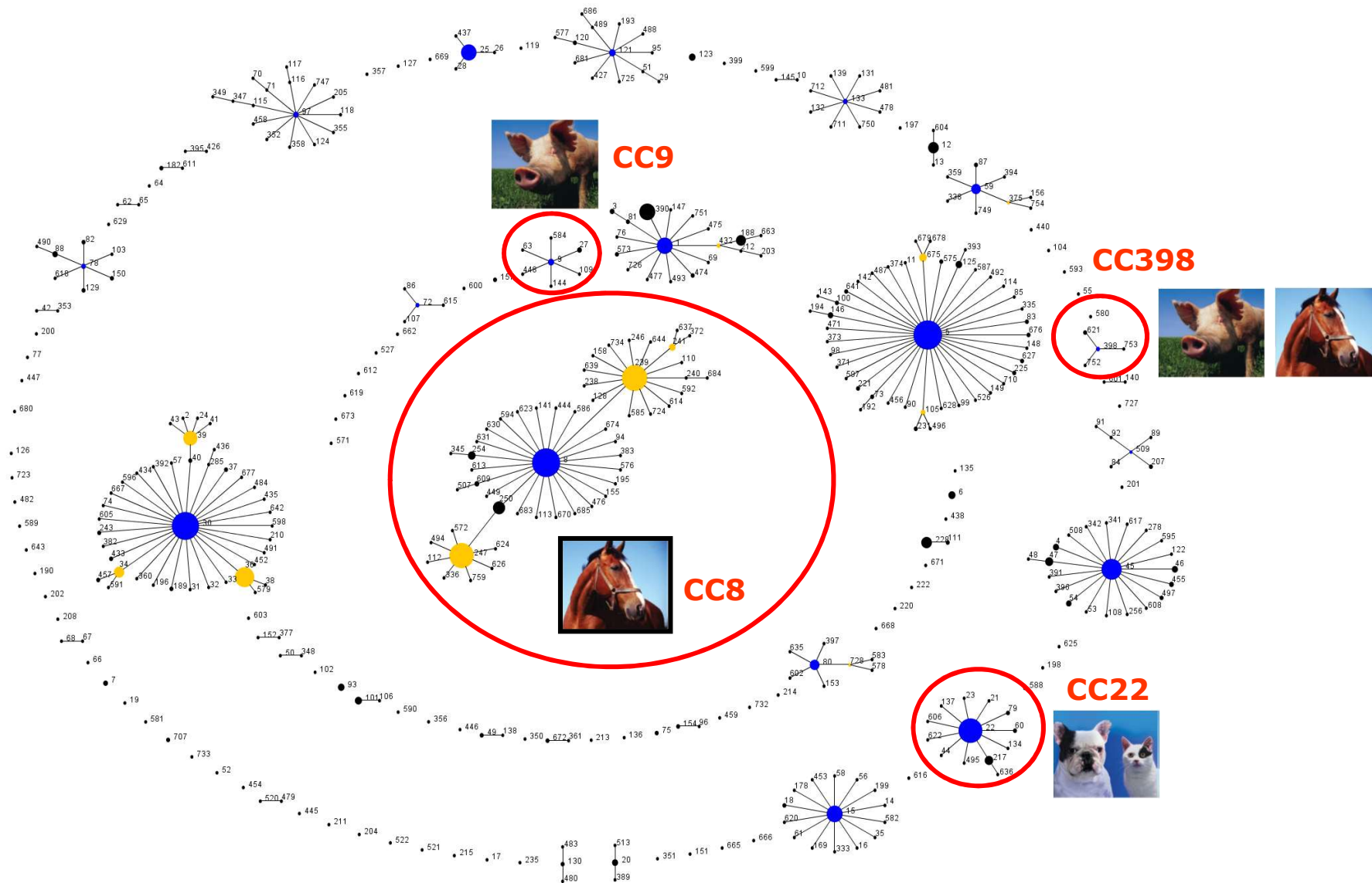
- MRSA stands for methicillin-resistant *S. aureus*, not 'multidrug-resistant *S. aureus*', i.e. some strains (not all) are multidrug-resistant.
- They are *S. aureus* strains that have acquired a methicillin resistance gene (***mecA*** or more rarely ***mecC***) conferring resistance to conventional  $\beta$ -lactams (penicillins & cephalosporins)
- Methicillin was used to treat penicillin-resistant *S. aureus* and cephalosporins were not yet discovered at the time MRSA were first reported (1960s)
- It spreads clonally with a few clones responsible for most human infections worldwide

## The impact of MRSA on human health

- 80,461 severe infections and 11,285 deaths per year in the US
- 171,200 (12%) bloodstream infections and 5,400 (37%) deaths per year in the EU



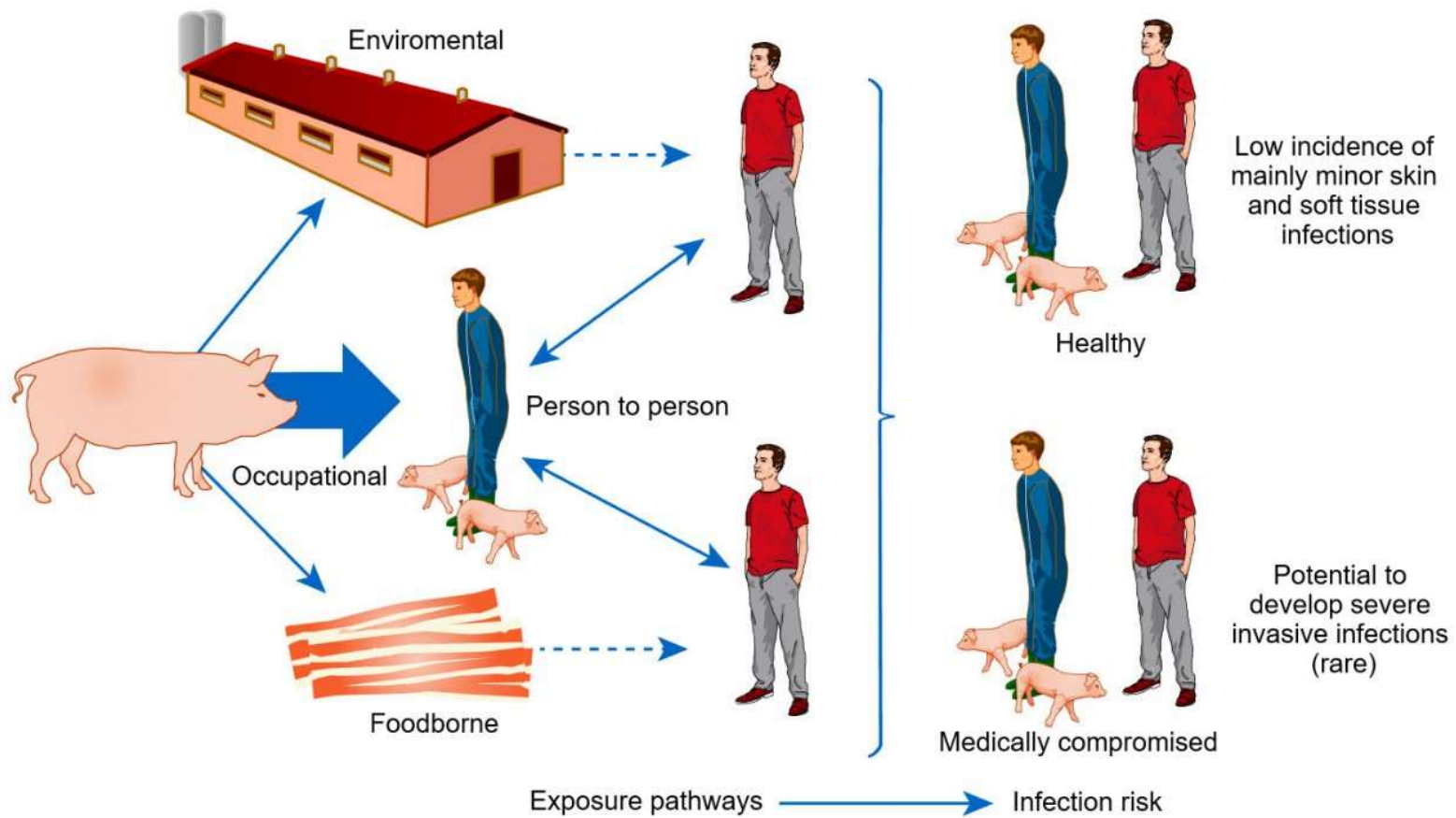
# MRSA population structure based on Multilocus Sequence Typing (MLST)



## LA-MRSA in pigs

- LA-MRSA ST398 was first reported in pigs in the Netherlands in 2005 (first retrospectively reported in Denmark in 2007 from isolates collected in 2005)
- All strains are resistant to tetracycline and zinc and various study have suggested that these agents have co-selected for LA-MRSA in pigs
- Usually the LA-MRSA strains found in a farm also occurs in the supplying farm
- The latest data from 2016 indicate a prevalence of 88% among Danish farms and 48% in Danish pork products
- Within positive farms, a minority (4-11%) of the pigs ("supercarriers") has stable high concentrations ( $\geq 10.0000$  CFU per swab)

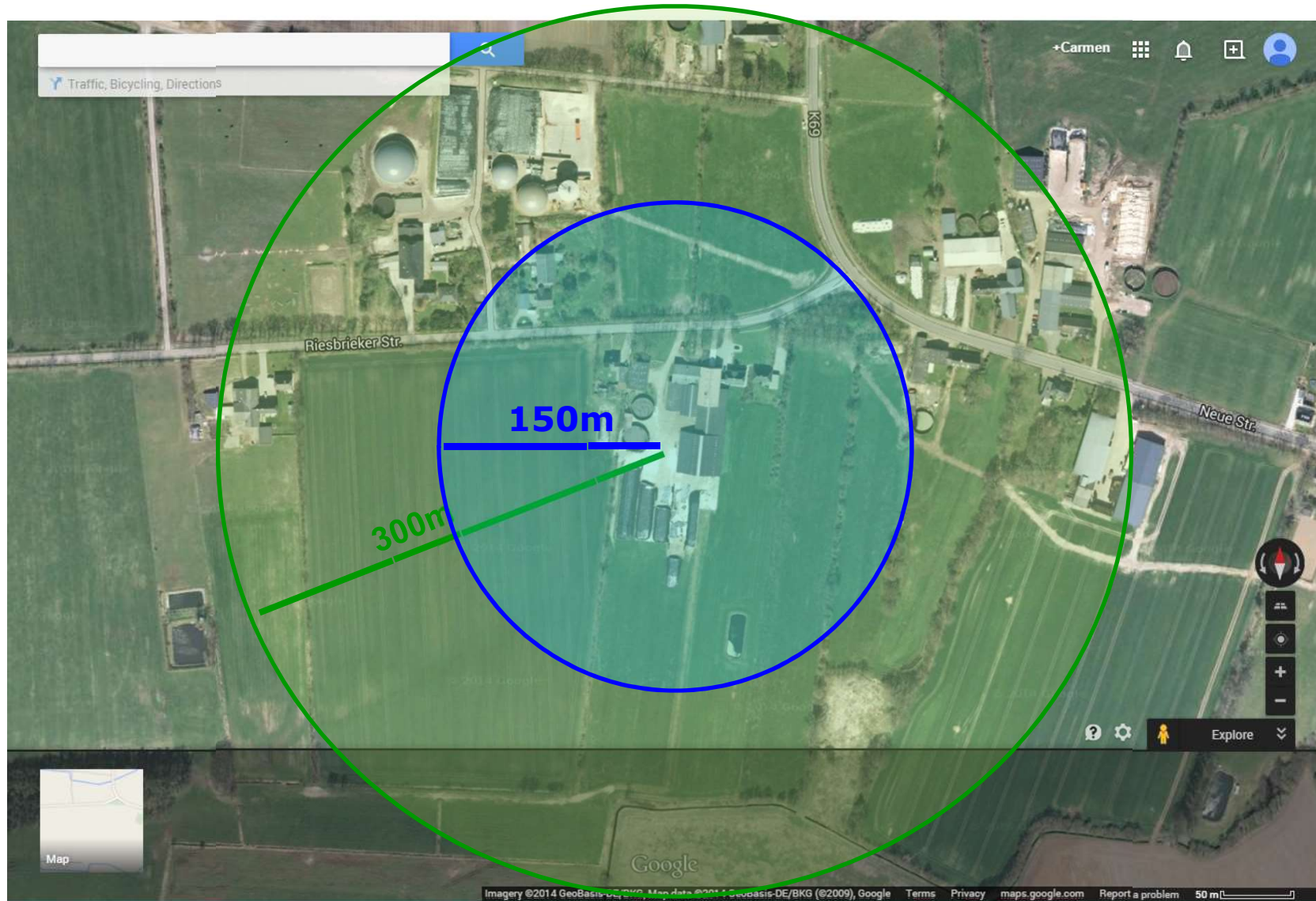
# Human exposure to LA-MRSA



## MRSA ST398 colonization in humans

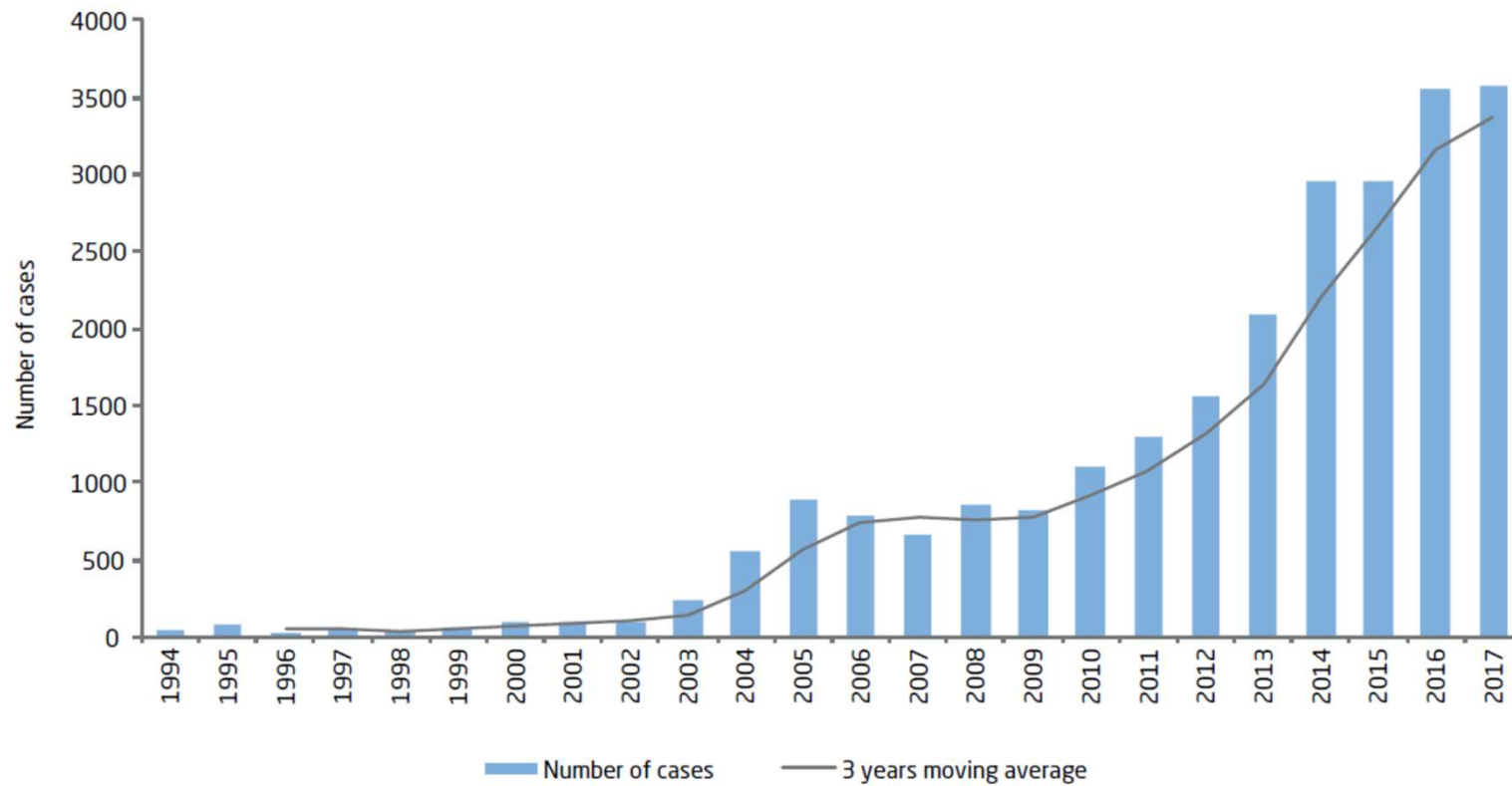
- Usually transient/unstable
  - 17% farm visitors become positive but 94% return negative after 24 h (van Cleef et al. 2010)
  - 58% reduction in farmers in the absence of exposure (Graveland et al. 2011)
- Limited spread from farms to the community
  - 86% positive farm workers and 4% family members
  - 45% positive veterinarians and 9% family members
  - <1% positive pupils from a local school (all living on pig farms) (Cuny et al. 2009)
  - 0.2% in animal-dense population areas (van Cleef 2010)

# Spread of MRSA ST398 in the vicinity of farms



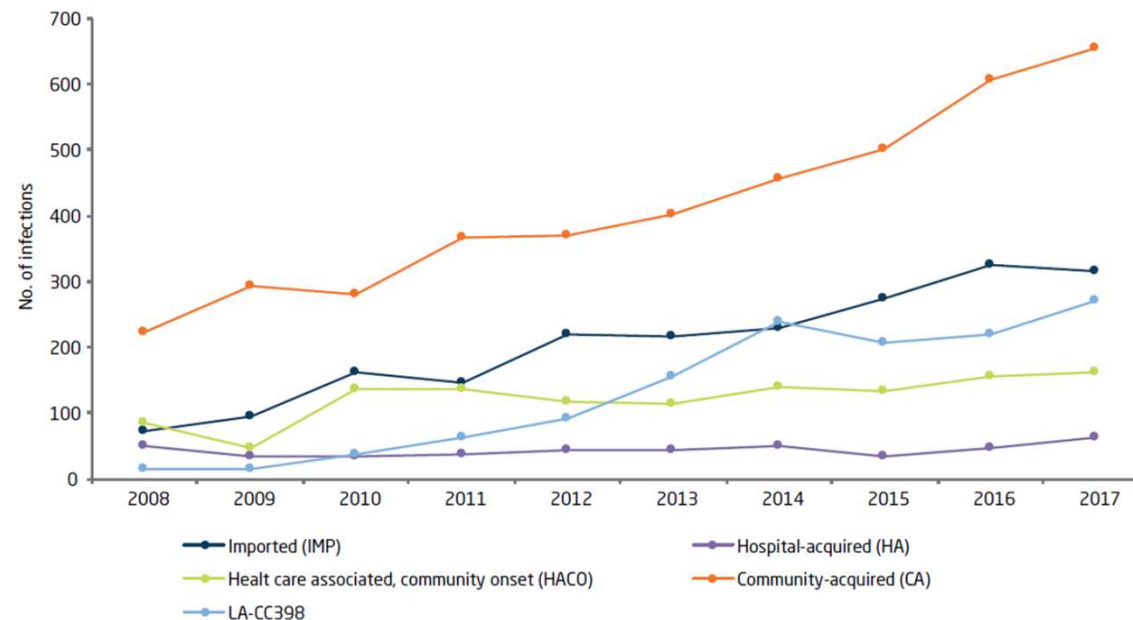
# Numbers of new MRSA cases in DK (1994-2017)

DANMAP 2017 ([www.danmap.org](http://www.danmap.org))



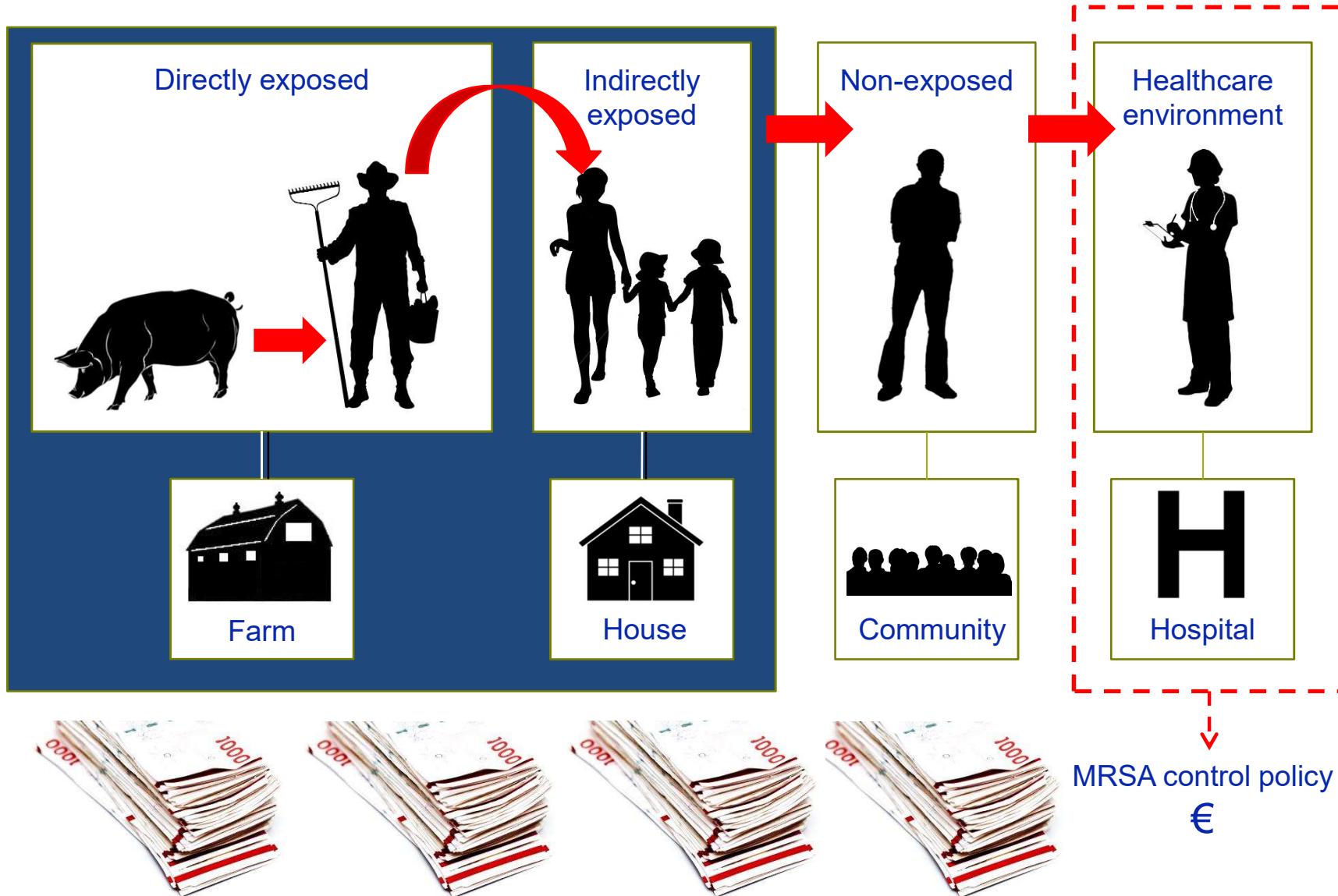
## Number of MRSA infections according to epidemiological classification

DANMAP 2017 ([www.danmap.org](http://www.danmap.org))



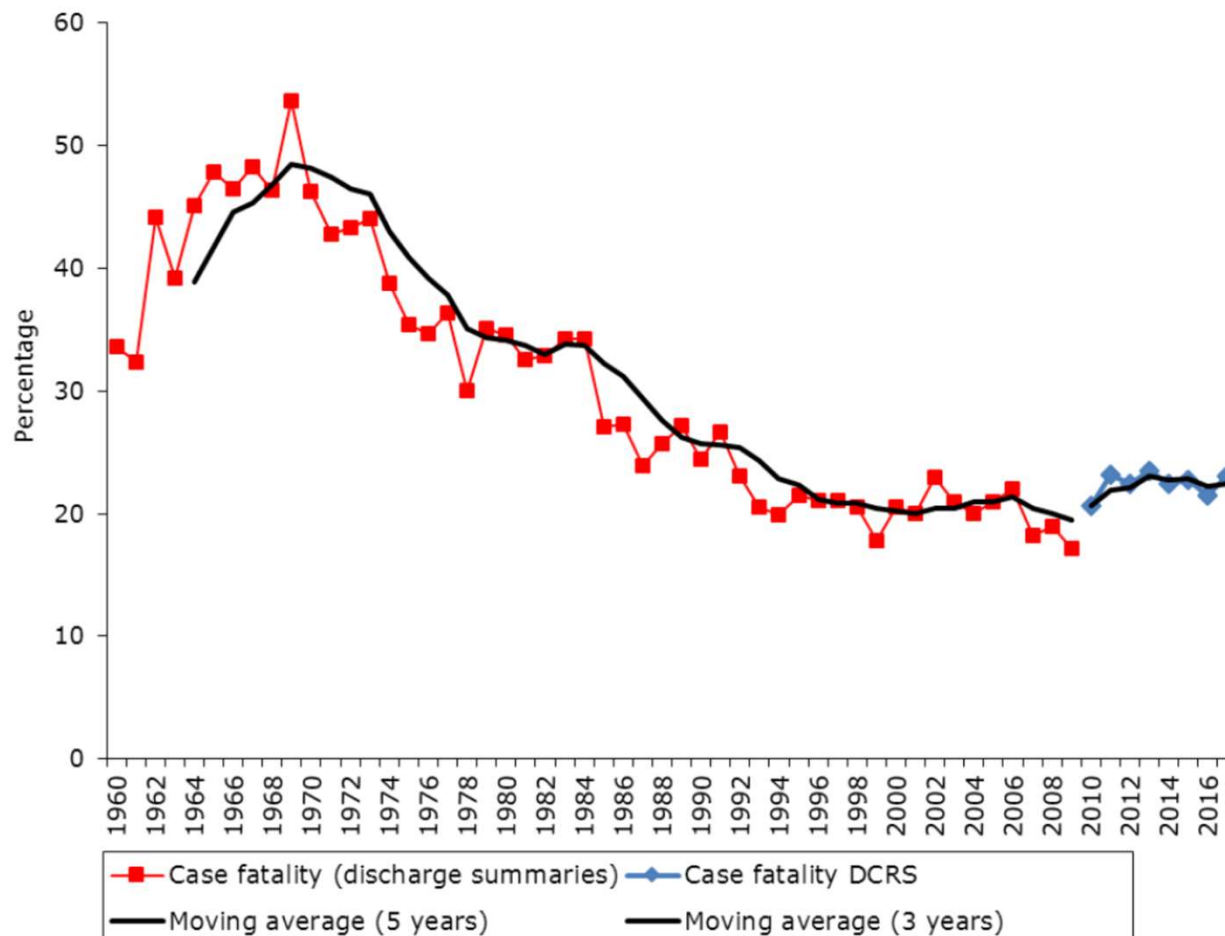
In 2017, people with contact to pigs comprised 84% of all new LA-MRSA cases, while the remaining 16% did not report any contact to pigs and thus may have been colonized or infected due to secondary transmissions

# The epidemiology of MRSA CC398



# Mortality of *S. aureus* bacteraemia in Denmark

## SAB report 2017



## MRSA vs. MSSA bacteraemia in DK

DANMAP 2014 ([www.danmap.org](http://www.danmap.org))

Impact	MRSA	All <i>S. aureus</i>
No. Infections	57 (3%)	1.964
Mortality	21%	22%
No. Associated deaths	12	437

MRSA causes less infections and has not higher mortality compared to MSSA

## LA-MRSA vs. other MRSA bacteraemia in DK

DANMAP 2014 ([www.danmap.org](http://www.danmap.org))

Impact	MRSA CC398	Total MRSA
No. Infections per year	8 (14%)	56
No. Associated deaths per year	<1	12

LA-MRSA causes 1/7 MRSA infections and has not higher mortality compared to other MRSA

## **S. aureus vs. E. coli bacteraemia in DK**

DANMAP 2014 ([www.danmap.org](http://www.danmap.org))

<b>Impact</b>	<b>S. aureus</b>	<b>E. coli</b>
No. Infections/cultures	1.964	4.500
% MRSA/ESBL	3%	7%
No. Associated deaths	437	Ca. 900

*S. aureus* infections are less common and less resistant to cephalosporins compared to *E. coli* infections. Besides this, there is a lack of effective new antibiotics against MDR Gram-negative bacteria, whereas numerous new anti-MRSA drugs are now available

# FORBRUG & LIV

Bolig Sundhed Digitalt Forbrug Biler Livsstil

SYGDOM 24. AUG. 2014 KL. 22.30

## Tusindvis er smittet med svine-MRSA uden at vide det

Op mod 12.000 danskere er uvidende om deres smitte med multiresistent svinebakterie.



# FORBRUG & LIV

Bolig Sundhed Digitalt Forbrug Biler Livsstil

SYGDOM 14. NOV. 2014 KL. 17.44

## Svine-MRSA koster endnu en person livet

I alt er to danskere nu døde af svinebakterien i 2014, oplyser Statens Serum Institut.



# FORBRUG & LIV

Bolig Sundhed Digitalt Forbrug Biler Livsstil

FORBRUGERSIKKERHED 6. OKT. 2014 KL. 18.00

## Snart kan vi dø af simple bakterieinfektioner

Antibiotika mister i stigende grad effekten på bakterier, der gør os syge. Siden 2012 er fire danskere døde af resistente MRSA-bakterier fra svin. Få et unikt indblik i antibiotika-resistens med professor og overlæge Hans Jørn Kolmos.



## Why is MRSA ST398 regarded as a big problem?

Denmark is a country with low MRSA prevalence

Denmark is one of the main pig producing countries

Search & destroy policy (€)

Incomplete & inaccurate communication?

## The communication black-out

Researchers overemphasize the problem to get public recognition, grants, etc.

Journalists make scary headings to sell newspapers

People get scared and pretend action

Politicians are under pressure and take action

Anybody Out There?



## Negative consequences of this black-out

- People are unnecessarily frightened
- People at risk (elderly) are not sufficiently informed
- Social consequences on MRSA patients and healthy carriers
- The research agenda is influenced by the media

### FORBRUG & LIV

Bolig Sundhed Digitalt Forbrug Biler Livsstil

SYGDOM 9. SEP. 2014 KL. 12.06

#### Kenneth blev smittet med svine-MRSA: »Folk reagerede som om, jeg havde pest«

33-årige Kenneth Sørensen har fået nok. Han vil ikke arbejde med svin længere.



# 35 mio. kr. sat af til kamp mod MRSA

SVIN · ØKONOMI | Onsdag 19. november 2014 | 10:00

Skrevet af [Landbrugsavisen.dk](http://Landbrugsavisen.dk)





**How big is the LA-MRSA  
problem in Denmark?**

## My personal opinion

- Relatively small compared to the emphasis given by the media and the actual burden caused by other MRSA, MSSA and *E. coli* infections
- Not negligible (tolerance zero)

## Take-home messages

- The pig MRSA is not the biggest AMR problem, just one among the others
- Other resistant bacteria that can be transmitted from animals are likely to pose a bigger risk to public health (stay tuned, next lecture 😊)
- The information provided by Danish media on pig MRSA was/is (?) often partial and inaccurate with negative consequences on society and research
- Responsibilities are shared between all parts involved in the public debate on MRSA, including researchers (everybody is biased!)